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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/177,814	10/23/98	GILTON	T	3530US(97-12

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EXAMINER	
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ART UNIT	PAPER NUMBER
1641	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/177,814	Applicant(s) Gilton
	Examiner Gailene R. Gab I	Group Art Unit 1641

[X] Responsive to communication(s) filed on *Apr 18, 2000*

[ ] This action is **FINAL.**

[ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle* 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

[X] Claim(s) *1, 3-64, 66-74, and 105-107* is/are pending in the applicat

Of the above, claim(s) ______ is/are withdrawn from consideration

[ ] Claim(s) ______ is/are allowed.

[X] Claim(s) *1, 3-64, 66-74, and 105-107* is/are rejected.

[ ] Claim(s) ______ is/are objected to.

[ ] Claims ______ are subject to restriction or election requirement.

Application Papers

[ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

[ ] The drawing(s) filed on ______ is/are objected to by the Examiner.

[ ] The proposed drawing correction, filed on ______ is [ ] approved [ ] disapproved.

[ ] The specification is objected to by the Examiner.

[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

[ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

[ ] All [ ] Some* [ ] None of the CERTIFIED copies of the priority documents have been

[ ] received.

[ ] received in Application No. (Series Code/Serial Number) ______.

[ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: ______

[ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

[X] Notice of References Cited, PTO-892

[ ] Information Disclosure Statement(s), PTO-1449, Paper No(s). ______

[ ] Interview Summary, PTO-413

[ ] Notice of Draftsperson's Patent Drawing Review, PTO-948

[ ] Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 4/18/2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/177,814 is acceptable and a CPA has been established. An action on the CPA follows.

Amendment Entry

2. Applicant's amendment and response filed 3/3/2000 in Paper No. 6 is acknowledged and has been entered. Claims 1, 4-5, 16-17, 30, 51, 57, 64, 66 and 72 have been amended. Currently, claims 1, 3-64, 66-74 and 105-107 are pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 1 as amended is vague and indefinite in reciting "a substrate **including** a material comprising ..." because it is unclear what other elements are included in the substrate other than silicon, gallium arsenide, and indium oxide.

Claim 1, as amended, is confusing in reciting “a matrix formed of said material of said substrate comprising...” because it is unclear what structurally differentiates or separates the claimed “substrate” from the “matrix” if both elements recited are formed of the same material. See also claim 57. Further, it is unclear what the structural and functional cooperative relationship is between the “substrate” and the “matrix” as claimed. See also claim 64.

Claim 5 is vague in reciting “a second porous region extending **a distance** across said substrate” because it does not specifically define the extent, as in length, of the distance crossed along the substrate, thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

Claim 10 is confusing and lacks antecedent support in reciting “**a first** reaction region... of said first porous region”. See claims 7, 8, and 9 for reference.

Claim 22 has improper antecedent basis problems in reciting “**a** first end...” and “**a** second end...”. See claims 19-21 for reference.

Claim 25 recites “a stationary phase disposed in said matrix” and claim 26 recites “(which) comprises a capture substrate”. It is unclear what the structural and functional cooperative relationship is between the “stationary phase” in these claims and the “reaction region (which) comprises a capture component” recited in claims 7, 8, and 9.

The phrase "at least a portion of" in claim 29 is a relative term which renders the claim indefinite. The phrase "at least a portion of" is not defined by the claim, the specification does

not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also claims 50 and 56.

Claim 30, as amended, is indefinite and indeterminate in scope in reciting "a substrate of a material" because it is unclear what material is encompassed by the claimed invention. See also claim 51.

Claim 30, as amended, has insufficient antecedent support in reciting "first porous matrix".

Claim 39 as amended is vague and indefinite in reciting "**including** a pump in communication with said at least one capillary column" because it is unclear what other elements are included in the capillary column other than the pump.

Claim 40 is indefinite and unclear in reciting "an end of said at least one capillary column" because it does not specifically define which end of the capillary column the valve is in communication with. See for example claim 42.

Claim 61 recites inconsistent language and has insufficient antecedent support in reciting "said first column and said capillary column".

Claim 71 recites "a reaction region along the length of said porous column". It is unclear what the structural and functional cooperative relationship is between the "reaction region" in this claim and the "capture substrate" recited in claims 66, 67, 68, and 69.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

4. Claims 1, 3-4, 7-9, 12, 18-20, 25-26, 29-32, 34-35, 38-39, 50-52, 56, 64, 66, 69, 71, and 73 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Isaka et al. (US 5,482,598).

Isaka et al. disclose a chromatograph apparatus comprising a microchannel element formed on a semiconductor substrate. Specifically, Isaka et al. disclose a chromatography apparatus which includes a semiconductor substrate and a matrix (microchannel) which extends across the substrate. The semiconductor substrate comprises of silicon (see column 6, lines 5-7). The matrix is formed with a desired pattern, i.e. linear, circular, on the semiconductor substrate by incorporating a porosity thereon in order to create a porous portion with increased pore size and extended branching of the pores on the semiconductor surface (see Abstract and column 1, lines 35-46). The length of the matrix channel is not limited although its length is preferably larger than its diameter (see column 2, lines 18-25). The porosity is preferably 10-90% (see

column 2, lines 60-63). Optimal pore size and pore shape can be achieved in accordance with the substance to be separated and measured, i.e. selecting the type and concentration of a dopant (see column 3, lines 35-42). A thin semiconductor substrate layer may be formed by ion injection after formation of a silicon dioxide layer by thermal oxidation (see column 4, lines 53-55). The chromatography apparatus comprising the matrix/microchannel element is applicable for use in solid-gas separation, solid-liquid separation, liquid-liquid separation, and gaseous separation. The separation makes use of the difference in flow rate between gases and liquids or in reactions (enzyme reaction) involving capture substrate (absorptivity involving immobilized enzyme) (see column 3, lines 1-14 and 50-54). In liquid chromatographs, an inlet port of the apparatus is coupled to a pump (migration facilitator) into the porous channel to identify difference in elution time between two liquids using differential refractometer (see column 5, lines 17-29). Isaka et al. also disclose ion column detection performed on a capillary, i.e. absorption detector (see column 3, lines 16-24). Finally, Isaka et al. teach incorporation of a sealing element (cover) consisting of a single-crystal silicon film on the silicon substrate on which the matrix is formed (see column 5, lines 38-49).

5. Claims 1, 18, 22-24, 30, and 42 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Northrup et al. (US 5,882,496).

Northrup et al. disclose fabrication and use of porous silicon structures to increase surface area of miniaturized electrophoresis devices and filtering or control flow devices (see Abstract).

Northrup et al. specifically disclose that porous silicon which is fabricated from crystalline silicon have very small pore diameters so that they can be produced with relatively high degree of uniformity and control (see column 1, lines 27-55). Northrup et al. teach that because of its high surface area and specific pore size, porous silicon can be utilized for a variety of applications on a miniature scale for significantly augmenting adsorption, vaporization, desorption, condensation, and flow of liquids and gasses while maintaining the capability of modification such as being doped or coated using conventional integrated circuit and micromachining (see Summary). Electrodes within or adjacent the porous membrane can be used to control flow or electrically charged biochemical species such as in electrophoresis (see column 5, lines 21-67). Figure 3 illustrates porous silicon embodiment on a controlled flow interface device. Figure 8 illustrates a porous silicon electrophoresis device. A negative electrode is formed at one end (inlet) of the porous silicon column and a positive electrode is formed is formed at an opposite end (outlet) of porous silicon columns, thereby forming microelectrophoresis channels (see column 7, lines 38-50).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 14-15, 16-17, 21, 40-41, 43-44, 54-55, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Miura et al. (US 5,132,012).

Isaka et al. has been discussed supra. Isaka et al. fail to teach specific detectors, processors, memory device, and controls incorporated in the chromatography apparatus.

Miura et al. disclose a miniaturized sample separator in the form of a liquid chromatograph comprising an analyzing chip in which the capillary flowpath is formed in a substrate and a field effect transistor detector disposed downstream of the capillary (see Abstract). The substrate is made of silicon and further has an insulative membrane formed of silicon dioxide (see column 3, line 51 to column 4, line 7). Both the column for separation and the field effect transistor are formed integrally with the substrate. After the silicon oxide layer has been formed on the capillary groove, a stationary phase is formed. A valve is connected to a first end of the flow path in the sample application area (sample introduction pipe) where a sample is selectively introduced into the flowpath. A separation carrier solution (carrier gas/ vacuum source) is fed under pressure by a feed pump and then discharged from a drain after having passed through the flowpath. Miura et al. further teach a sealing element (seal plate) such as borosilicate glass for sealing the opening portion of the groove portion to define the flow passage for a liquid sample. The liquid chromatograph also comprise a memory (control) device and an output device such as a data processor which is connected to the detector for detecting separated constituents (see column 5, line 63 to column 6, line 22). Figures 4A and 4B illustrate an electrical conductivity detector which comprise voltage application and current detection

components, i.e. electrodes. Figure 9 shows a schematic view of the overall flow passage of the liquid chromatograph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate specific chromatography device elements such as taught by Miura into the chromatograph apparatus with porous silicon channels as taught by Isaka because Miura specifically indicated difficulty in miniaturization of liquid column chromatographs and Isaka specifically taught possibility of miniaturization of apparati through the use of porous silicon because porous silicon has established porosity which greatly enhances capacity for separation in the miniature scale. One of ordinary skill in the art at the time of the invention would have been motivated to incorporate the specific detectors, processors, memory device, and controls in the chromatograph device as disclosed by Miura into the chromatograph apparatus of Isaka because Miura recognized and solved technical difficulties in miniaturizing analyzers by incorporating all the necessary elements into the device (rather than providing them independently of each other) and Isaka recognized and specifically taught further advancement introduced through the use of porous silicon in significantly enhancing separation, augmenting adsorption, differentiating flow rate in liquid or gaseous samples in apparati of miniature scales.

7. Claims 13, 21, 41, 53, and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Wang et al. (US 5,663,488).

Isaka et al. has been discussed supra. Isaka et al. fail to teach integration of a migration facilitator and thermal detector into the chromatography apparatus.

Wang et al. disclose a migration facilitator (pumping assembly) incorporated into a separation column and thermal device for use in selective control of thermal isolation of the thermal zone as well as effecting selective amount of gas pressure in an enclosed cavity (see Abstract). The pumping element comprises an element in the form of a tubular or planar palladium structure. Wang et al. disclose that the migration facilitator controls the extent of thermal isolation by changing the gas pressure in the cavity thereby changing the amount of heat transfer between the separation column and housing so as to reduce the need for operation of the thermal device (see column 2, lines 1-54). The migration facilitator also includes a control (check) valve for venting or purging gasses form the closed cavity, a vacuum (or near vacuum) source for use in high vacuum pumps for altering the concentration of gas within the cavity volume (see column 4, lines 4-59). Wang further disclose that a thermal conductivity detector is integrated into the chromatograph for determining physicochemical properties of the fluid stream which exits the separation column (see column 10, line 60 to column 11 line 33).

It would have been obvious to one of ordinary skill in the art at time of the invention to incorporate a migration facilitator and a thermal detector as taught in the analytical instrument of Wang into the chromatograph apparatus with porous silicon channels as taught by Isaka because Wang specifically suggested application of his pump assembly to miniaturized chromatographic apparati capable of regulated flow such as taught by Isaka. One of ordinary skill in the art at the

time of the invention would have been motivated to incorporate the migration facilitator and thermal detector as taught in the device of Wang in a chromatographic device such as taught by Isaka because Isaka specifically taught that porous silicon has established porosity with enhanced capacity for separation in the miniature scales; therefore, the advantage achieved in its use for enhancing separation, augmenting adsorption, differentiating flow rate in liquid or gaseous samples in apparati of miniature scale is further heightened by effecting selective pressurization and thermal isolation such as taught by Wang.

8. Claims 33, 74, and 105-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Turner et al. (US 5,885,869).

Isaka et al. has been discussed supra. Isaka et al. fail to teach specifically teach incorporation of hemispherical grained silicon into the separation columns.

Turner et al. disclose a method which enables uniformly doping hemispherical grain polycrystalline silicon (HSG) or a top roughened polysilicon layer independent of other layers in a semiconductor substrate (see Abstract). Initially, a semiconductor substrate having a silicon dioxide layer formed superadjacent a polycrystalline layer is provided, preferably in a chamber. Subsequently, a doped rough silicon layer is formed in situ superadjacent the silicon dioxide layer which is accomplished by depositing a silicon layer superadjacent the silicon dioxide layer and exposing the silicon layer to a source gas. The step of roughening is achieved by vacuum

annealing an amorphous layer using rapid thermal chemical vapor deposition techniques or low pressure chemical vapor deposition (see column 3, lines 7-23).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the teaching of Turner in doping hemispherical grained silicon into the chromatograph apparatus with porous silicon channels as taught by Isaka because Isaka specifically taught that porous silicon has established porosity which greatly enhances capacity for separation in the miniature scale and Turner specifically suggested forming a doped rough silicon layer superadjacent a silicon dioxide layer in a semiconductor substrate such as taught by Isaka in the formation porous silicon channels in a microchannel element of a miniaturized chromatograph. One of ordinary skill in the art at the time of the invention would have been motivated to incorporate the teachings of Turner in doping hemispherical grained silicon into the miniaturized separation device of Isaka because Isaka recognized and specifically taught advantage introduced through the use of porous silicon, such as HSG, in significantly enhancing separation, augmenting adsorption, differentiating flow rate in liquid or gaseous samples in apparati of miniature scales.

9. Claims 5-6, 10-11, 27-28, 36-38, 45-49, 57-63, 67-68, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) or if necessary, Northrup et al. (US 5,882,496) in view of Turner et al. (US 5,885,869) and in further view of Sunzeri (US 5,536,382) and Swedberg et al. (US 5,571,410).

Isaka et al., Northrup et al. and Turner et al. have been discussed supra. Isaka et al., Northrup et al., and Turner et al. fail to teach use of internal reference or control. Isaka et al. further fail to teach biocompatible porous medium of particles incorporated into the stationary phase such as antigens antibodies for use as capture system.

Sunzeri discloses analysis of constituents of human biological fluids using capillary electrophoresis. Sunzeri specifically teaches the use of standard control to provide a standard for quantitation (see column 9, lines 28-67). Sunzeri further teaches that quantitation using internal and external standards is beneficial in assays where the sample matrix affects fluorescence sample quenching (see column 10, lines 1-34).

Swedberg et al. teach a miniaturized planar column device for integrated sample analysis of analytes (see column 8, lines 5-38). Swedberg et al. specifically teach a stationary phase (sample treatment component) which performs a filtration function filled with a biocompatible porous medium of particles into which a capture function has been incorporated therein (see column 27, lines 33-61 and Example 1). Swedberg et al. also disclose a "LIGA" process which is used to refer to a process of fabricating microstructures having high aspect ratios and increased structural precision in order to create desired uniformity in microstructures such as channels ports, apertures, and microalignment means (see column 13, lines 9-33).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the stationary phase in the porous matrix of the chromatographic separation apparatus taught by Isaka or Northrup, with HSG as taught by Turner and incorporated therewith, one that

effects biocompatibility into the matrix, i.e. antigens and antibodies, as taught by Swedberg in order to achieve performance of both filtration and capture function because Swedberg specifically suggested potential application of his teachings in monitoring biological analyses as applied to liquid phase separation devices in the miniature scales. One of ordinary skill in the art would have been motivated to incorporate the teachings of Turner and Isaka or Northrup, with biocompatible modification as taught by Swedberg because Isaka specifically taught that porous silicon has established porosity with enhanced capacity for separation, augmented adsorption, differentiation of flow rate in liquid or gaseous samples, thereby producing a highly versatile miniaturized chromatographic device capable of both enhanced partitioning and complexation reactions. Furthermore, with the advent of silicon micromachining and LIGA in the teachings of Swedberg, one of ordinary skill in the art would have reasonable expectation of success in fabricating multiple separation columns or channels with a high degree of uniformity and precision in order to allow accurate comparative and correlative measurement of sample results in comparison to internal controls, references, or standards with known measurement levels as those taught by Sunzeri, because quality control monitoring is a standard practice and a well known art for monitoring the functionality, accuracy, and precision of various laboratory apparati.

Response to Arguments

10. Applicant's arguments with respect to claims 1, 3-64, 66-74, and 105-107 have been considered but are moot in view of the new grounds of rejection. No claims are allowed.

Remarks

11. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Yu (US 5,583,281) discloses a miniature gas chromatograph comprising a silicon wafer, a gas injector, a column and a detector. The column is a microcapillary in silicon crystal with a stationary phase and is mechanically connected to receive a mobile phase from the gas injector for molecular separation of compounds in a sample gas (see Abstract). The mobile phase is a carrier gas or inert gas, usually nitrogen, hydrogen, helium, or argon (see column 2, lines 28-42).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

5/18/00

Gailene R. Gabel
Patent Examiner
Art Unit 1641

James C. Housel
JAMES C. HOUSEL 5/22/00
SUPERVISORY PATENT EXAMINER